A STUDY OF OCULAR MANIFESTATIONS IN SYSTEMIC LUPUS ERYTHEMATOSUS

DISSERTATION SUBMITTED FOR

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CERTIFICATE

This is to certify that the dissertation entitled **"A STUDY OF OCULAR MANIFISTATIONS IN SYSTEMIC LUPUS ERYTHEMATOSUS"** presented herewith by ***Dr. R. KALADEVI*** to the faculty of Ophthalmology, The Tamilnadu Dr. M.G.R. Medical University, Chennai in partial fulfillment of the requirement for the award of M.S. degree in Ophthalmology is a bonafide work carried out by her under my direct supervision and guidance.

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DECLARATION

I, **DR.R.KALADEVI,** *solemnly declare that the dissertation titled* ***"A STUDY OF OCULAR MANIFESTATIONS IN SYSTEMIC LUPUS ERYTHEMATOSUS"*** *has been prepared by me*.

This is submitted to The Tamil Nadu Dr.M.G.R. Medical University, Chennai, in partial fulfillment of the requirements for the award of M.S Degree Examination (Branch III) Ophthalmology to be held in SEPTEMBER 2006 .

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INTRODUCTION

Systemic Lupus Erythematosus is a chronic progressive autoimmune disease with multisystem manifestation.

The underlying abnormalities in systemic lupus erythematosus is due to the production of a number of pathogenic autoantibodies and immune complexes and to an inability to suppress and clear them. The disease can present in a wide variety of forms, degrees, and manifestation, ranging from relatively mild cutaneous and joint involvement to lethal cardiac, renal and cerebral involvement.

Systemic lupus erythematosus commonly presents in young and middle aged woman who comprise upto 90% of all systemic lupus erythematosus sufferers. Systemic lupus erythematosus is three times more common in blacks than in other races and Asians display an increased incidence of systemic lupus erythematosus against Caucasians.

HISTORY

In 1852 Cazenave and Chausit[5] were the first to use the new famous name Lupus erythematosus and to describe a number of systemic manifestation of this condition.

In 1939 Rose and Pillsbury[31] described disseminated multiorgan involvement in this chronic progressive disease of unknown etiology. Their report was considered the beginning of modern history of systemic lupus erythematosus.

In 1941 Klemperer and coworker[19] published their article on Pathology of Disseminated Lupus erythematosus again emphasizing the importance of vasculitis as a central feature of systemic lupus erythematosus.

In 1964 Halmay and Ludwig[16] described a case of deep band shaped white grayish coloured keratitis with hyaline granular aspect apparently with involvement of descement membrane. This was associated with uveitis in patient with lupus whose cutaneous manifestation were simultaneous with ocular findings.

In 1993 Varga and Wolf[39] described the case of systemic lupus erythematosus with extensive impairment of the CNS and bilateral transient keratoendothelitis responsive to topical and systemic corticosteroids.

PATHOPHYSIOLOGY

Systemic lupus erythematosus is a dysfunction in immunoregulation in an individual genetically predisposed to have such dysregulation triggered by an environment agent such as microbe or a drug or other chemical. The immunopathology is related primarily to B lymphocyte hyperactivity although T cell abnormalities are seen as well. Numerous antibodies and immune complexes that cause specific tissue damage are produced, however not all antibodies are pathogenic.

Additionally other immunoregulatory mechanisms are abnormal in systemic lupus erythematosus including T – lymphocyte numbers and function and the inability to clear antibodies and immune complexes. Auto antigen – autoantibodies and immune complexes formed in systemic lupus erythematosus patients are deposited at certain loci in “target tissues” and can lead to subsequent complement activation, inflammatory cell chemotaxis to the site of the immune complex. Release of proteolytic and collangenolytic enzymes from these cells result in tissue digestion and damage.

A genetic predisposition with high concordance of disease in monozygotic twins as compared to dizygotic twins and an increased frequency of family members affected with systemic lupus erythematosus. There are

associations with class II HLA genes including HLADR2 and HLADR3 particularly HLA-DRB-I *0301 allele and DQA –I * 0501 allele. These HLA regions exert certain effect on certain autoantibodies. Complement genes C4A, C4B also play important role. Genetic studies show that the defect is in the region of chromosome 6 were the putative immune response genes is located.

Systemic lupus erythematosus vasculitis often shows nonspecific pathological changes. Findings include fibrinoid necrosis of small vessels and capillaries and deposition of immunoglobulin and complement. Lupus anticoagulants may initiate clotting within blood vessels.

In the eye, the immune complexes deposit in the vascular endothelium of conjuctiva, sclera, choroids, ciliary body and retina, alter the tissue structure and compromise function. Deposit can also develop in the basement membrane of the ciliary body and conjuctiva. While most patients with retinopathy have systemic disease, retinopathy can also occur independently of systemic flare-ups. Systemic lupus erythematosus patients with retinopathy have higher morbidity risk.

ENVIRONMENTAL FACTORS

VIRAL INFECTION : Systemic lupus erythematosus is caused by an inappropriate immune response to viral infection, namely Type C virus of reoviridae family. This virus has particular tropism for thymus cells. The virus incorporates the genome into the host genome. On multiplication the altered DNA provoke antibodies against itself. Thus thymic dysfunction and disturbed immunoregulation, molecular mimicry plays important role.

UVRADIATION

DRUG: Hydrazine Procainamide Methyldopa Isoniazid

HORMONAL FACTORS:

More in females and more in pregnant women. Estrogen enhances the disease and testosterone suppresses it.

SYSTEMIC MANIFESTATION OF

SYSTEMIC LUPUS ERYTHEMATOSUS

The various systemic manifestation divided into constitutional renal dermatologic, neurological, ophthalmic, and others.

CONSTITUTIONAL SYMPTOMS :

Prominent constitutional symptoms include fever, malaise, arthralgia, myalagia, headache, loss of appetite and weight.

Skin findings include the typical malar butterfly rash, discoid lesions, non specific crythematous maculopapular rash, and cutaneous vasculitic lesion.

RENAL MANIFESTIONS :

This is the most common manifestation.[36] All patients of systemic lupus erythematosus have deposits of immunoglobin, in glomeruli, one half of patients have clinical nephritis defined by persistent protenuria.[15] Most patient are asymptomatic except those with edema of nephrotic syndrome. Urine analysis shows haematuria and protenuria. They present with mesangial or mildfocal glomerulonephritis. Patients with high proportion of sclerotic

glomeruli on biopsy, usually have serum creatinine of more than 265 micromols per litre are unlikely to respond to immunosuppressive therapy.

DERMATOLOGICAL MANIFESTATIONS:

Dermatological features play a prominent role in the diagnostic scoring system and are second most common manifestation.[36]

The pathognomonic lupus or butterfly rash across the nose and cheeks occurs in some 30% of patients with systemic lupus erythematosus. Discoid or disc shaped skin lesion may also occur in systemic lupus erythematosus and discoid lupus erythematosus. They begin as erythematosus macules, expand to plaques but always retain their discrete coin shape. They occur on extensor surface of arms and on neck, face and scalp. They occur in 15 to 30% of patient with systemic lupus erythematosus. Photosensitivity rash is also typical with systemic lupus erythematosus with sunburn of extreme severity. Livedo reticularis is seen in systemic lupus erythematosus patients with frank vasculitis or in those individuals with anticardiolipin antibodies. Alopecia is another manifestation. Other manifestations are raynaud phenomenon, oral nasal or other mucous membrane ulceration and telengiectasias may occur.

NEUROLOGICAL MANIFESTATIONS :

Neurological manifestations of lupus are seen in 25 to 75% of patients and can involve all parts of nervous system. The neurological manifestations were similar in systemic lupus erythematosus and connective tissue disorder and a positive correlation is seen with antiphospholipid antibodies and anticardiolipid antibodies. The various manifestations are personality disorder, seizures, psychosis, stroke and migrainous headache.

PREGNANCY AND LUPUS :

Pregnancy and lupus is complicated by high rate of spontaneous abortions and stillbirth and flare up of the disease with resulting fetal loss and fetal growth retardation. Congenital lupus includes discoid lupus and congenital heart block often detected in-utero.

DRUG INDUCED SYSTEMIC LUPUS ERYTHEMATOSUS

The drugs implicated in systemic lupus erythematosus are procainamide, hydralizne, isoniazid, chlorpromazine, pencillamine, practolol, methyl dopa, oral contraceptive pills and propylthiouracil. Patients with drug induced systemic lupus erythematosus are woman presenting with polyarthritis, pleuritis or Pericarditis. Anti histone anti bodies are usually present.

SYSTEMIC LUPUS ERYTHEMATOSUS AND OTHER AUTOIMMUNE DISEASES:

The following autoimmune diseases are associated namely autoimmune thyroid disease, hereditary C1Q deficiency, SS-systemic sjogren syndrome.

OCULAR MANIFESTATIONS OF

SYSTEMIC LUPUS ERYTHEMATOSUS

EXTERNAL:

- KERATOCONJUCTIVITIS SICCA
- CONJUCTIVITIS
- SUPERFICIAL PUNCTATE KERATITIS
- INTERSTITIAL KERATITIS
- EPISCLERITIS AND SCLERITIS

RETINAL MANIFESTATION:

- COTTON WOOL SPOTS
- HAEMORRAGES
- BRANCH RETINAL VEIN OCCLUSION
- CENTRAL RETINAL VEIN OCCLUSION
- CENTRAL RETINAL ARTERY OCCLUSION
- RETINALVASCULITIS
- PROLIFERATIVE RETINOPATHY

CHOROIDAL MANIFESTATION:

- ISCHEMIC CHOROIDAPATHY
- RETINAL PIGMENT EPITHELIAL CHANGES
- CHOROIDAL VASCULITIS

NEURO OPHTHALMIC AND ORBITAL MANIFESTATION:

- OPTIC NEURITIS
- ISCHEMIC OPTIC NEUROPATHY
- PSEUDOTUMOUR CEREBRI
- MIGRAINE
- HEMIANOPIA AND AMAUROSIS
- VISUAL HALLUCINATIONS
- GENICULOCALCARINE BLINDNESS
- PUPILLARY AND OCULOMOTOR DISTURBANCE
- INTERNUCLEAR OPHTHALMOPLEGIA
- ORBITAL PSEUDOTUMOUR
- ORBITAL MYOSITIS

The most common ocular manifestation of systemic lupus erythematosus is keratoconjuctivitis sicca with or without xerostomia[35] occurs in approximately 25% of patients. Keratoendothelitis causing transient corneal edema has been noted.[41] The lesions responded well to Quinacrine hydrochloride. Diffuse anterior or nodular scleritis closely may mimic the level of systemic activity in the disease. Periorbital edema is a rare manifestation of the disease.

LIDS AND CONJUNCTIVA:

Patients can present with non specific blepharitis without scarring. Other lesions are lid plaque, lid scarring, symblepharon formation. They responded well to topical steroids but in patient with more extensive bilateral involvement these have recurred as treatment was reduced. Chemosis may be the initial presentation in systemic lupus erythematosus patients.

CORNEAL MANIFESTATIONS :

The corneal manifestations of systemic lupus erythematosus are by large confined to epithelium. Peripheral ulcerative keratitis have been reported in patients with systemic lupus erythematosus. Sicca syndrome is quite common .Gold and his associates found a 6.5% incidence of keratitis in an outpatient

population of systemic lupus erythematosus patients. Spaeth studied that 88% of systemic lupus erythematosus patients revealed superficial punctate keratitis with fluorescein corneal staining.[33] Schrimer test were normal in these patients .Therefore the superficial punctate keratitis seen in these patients are due to dry eye states or due to the disease process itself is under investigation. A case of bilateral deep segmental interstitial keratitis, a rare finding has also been reported.[29]

SCLERAL INVOLVEMENT:

Recurrent episcleritis, scleritis may be the initial presentation in systemic lupus erythematosus. Scleritis mimics the level of systemic disease and it resolves with adequate control of systemic disease and it will not respond to topical therapy.

UVEAL INVOLVEMENT:

Uveitis is an uncommon manifestation. Patient presents with pain, photophobia and diminished vision. On examination there is corneal edema, flare, cells, keratic precipitates and fibrinous membrane. Response is good with steroids hence vision loss prevented.

RETINAL MANIFESTATIONS :

Retinal involvement in systemic lupus erythematosus is quite common, second only to keratoconjunctivitis sicca. The reported prevalence has varied greatly between patients in precorticosteroid era and ambulatory systemic lupus erythematosus patients with better control of the disease. The appearance and disappearance of retinal lesions in patients with systemic lupus erythematosus parallels the systemic clinical course. Effective control of systemic disease is associated with dramatic decrease in retinal lesions.[13] Moreover systemic lupus erythematosus patients with retinopathy have decreased survival rate compared to systemic lupus erythematosus patients without retinopathy.[34] Patients are usually asymptomatic and rarely complain of loss of vision and scotomas.

RETINAL VESSEL SHEATHING :

They are focal fluffy white cuffing which develop around long stretched vessels. They may be continuous more around the veins than arteries.

Pathogenesis:

Circulating leucocytes must slow down and adhere to the vascular endothelium. This is brought about by the adhesion molecules. Initial adhesion by L selectin and carbohydrate slows the leucocyte. Once tethered they stimulate P selectin and E selectin, adhere to the carbohydrate moiety called

addresins in the vascular endothelium. Firm adhesions of the leucocyte by interaction of its integrin receptors latch the cell on the vessel wall. This results in activation of leucocytes and flattening of cell. Binding of cell adhesion molecules on the endothelium initiates migration. These cells migrate out of the endothelium into extracellular matrix and bind to beta-integrins in the extra cellular matrix and form perivascular cuffing.

COTTON WOOL SPOTS:

The classic finding in lupus retinopathy is cotton wool spots. They represent areas of microvascular occlusion. They may be isolated or surrounded by haemorrage. They are due to focal areas of ischemia due to interruption of axoplasmic flow in the nerve fibre layer of retina, resulting in accumulation of axoplasmic material and swelling of nerve fibre layer, probably due to occlusion of precapillary arteriole or end arteries by thrombus or inflammatory cells. FFA correspond to focal areas of nonperfusion .Histology reveals focal swelling of nerve fibre layer with cytoid bodies .DD: diabetes, hypertension, ischemic retinal vein occlusion.

The pathological finding in lupus retinopathy includes infiltration of vessel wall with fibrillar material causing vascular constriction and widespread hyaline thrombus formation. Although focal areas of vessel wall infiltrates are seen, the vessel wall themselves are free of inflammatory cells. This is not a

true vasculitis. This type is associated with active systemic disease and CNS lupus.

ARTERIAL OCCLUSION:

It is rare for lupus retinopathy. More common in patients with antiphospholipid antibodies. Features result in central retinal artery occlusion, extensive capillary nonperfusion and retinal neovascularisation may occur. This is associated with active systemic disease and CNS lupus.

VENOUS OCCLUSION:

Systemic lupus erythematosus is not a venous disease. Arterial occlusion secondarily causes venous stasis and engorgement of veins with a picture resembling central retinal vein occlusion. Acquired protein S deficiency is also reported in systemic lupus erythematosus.

VASODISRUPTION:

Intra retinal haemorrages are frequent finding in lupus retinopathy. Microaneurysm formation, vascular leakage, retinal edema, preretinal haemorrage can also occur. Studies have proven that increased intraretinal haemorrage is proportional to increased risk of mortality.

ISCHEMIC SEQULAE:

Features of hypertensive retinopathy like arteriolar attenuation, arterio venous crossing changes, intra retinal haemorrage hard exudates can occur.

Sometimes systemic lupus erythematosus patients may present with bilateral mottled retinas with spots or clumps of pigments which may resemble those patients with retinitis pigmentosa. These may be due to vasoocclusive phenomenon.

The data has indicated that if retinal vasculitis exists in a patient with systemic lupus erythematosus, then the renal, pulmonary and cardiovascular status of the patient will be the next to suffer the consequences of immune complex vasculitis as illustrated by el-Asrar and Associates.

CHORDOIAL INVOLVEMENT:

Choroidopathy is much less common in systemic lupus erythematosus as compared with retinopathy. A case of bilateral serous detachment has been reported in systemic lupus erythematosus. Transudation of fluid is seen through bruch's membrane and the retinal pigment epithelium which appears to be affected by ischemia, may be due to immune complex deposits in bruch membrane. The presence of antineuronal antibodies found in serum and CSF of systemic lupus erythematosus patients has led them to speculate the existence of anti retinal pigment epithelial antibodies. Sometimes choroidal infarction

with occlusive vascular disease leads to irreversible blindness - “ELSCHNIG SPOTS.” Immunopathological studies have shown extensive deposits of immune complexes in the choroid probably because of profuse blood flow. Others include extensive mononuclear cell inflammatory infiltrate .Although more extensive changes are seen in lupus in choroids than retina they are always subclinical.

NEURO OPHTHALMIC INVOLVEMENT:

The neuro ophthalmological manifestations have been reviewed by LESSEL.[23] The optic nerve and chiasma may be involved in systemic lupus erythematosus most likely by an ischemic process. Anterior or posterior ischemic optic neuropathy or a picture similar to optic neuritis has been reported. Pathological findings include demyelination, axonal necrosis or a combination of both. These findings are associated with antiphospholipid antibodies.

Disc edema in lupus may be secondary to hypertension, central retinal vein occlusion, focal ischemic disease, increased intra cranial tension, or transverse myelitis. A clinical picture similar to pseudotumour cerebri has also been reported.

Retrochiasmal visual problems in lupus include geniculocalcarine blindness, homonymous hemianopia, visual hallucinations and transient

amaurosis. Patients with systemic lupus erythematosus are prone to migraine and amaurosis in systemic lupus erythematosus and respond better to nifidipine suggesting a vascular etiology. Manifestation consistent with Miller Fisher Syndrome in systemic lupus erythematosus (ataxia, areflexia, ophthalmoplegia) has also been reported.

The pupillary abnormalities in systemic lupus erythematosus are secondary to brain stem lesions. Painful ophthalmoplegia reversed by steroids are seen in systemic lupus erythematosus patients .Diplopia is transient phenomenon often with vertigo can be seen suggesting vestibulobasilar insufficiency .Unilateral internuclear ophthalmoplegia is well documented with systemic lupus erythematosus. Isolated ptosis and isolated sixth nerve palsies are also reported.

OTHER OPHTHALMIC INVOLVEMANT:

Orbital involvement mimics pseudotumour cerebri and there is a good response to steroids. Orbital myositis manifesting with proptosis, pain with external ocular movements restriction have been noted. Reports of concomitant development of Brown syndrome have also been noted. Often this is the cause of vertical diplopia in patients with systemic lupus erythematosus.

SYSTEMIC INVESTIGATIONS

ROUTINE BLOOD INVESTIGATIONS

- Total count
- Red blood cell count
- Differential count
- Erythrocyte Sedimentation Rate
- Findings may include anaemia, leucopenia, lymphopenia, thrombocytopenia and Erythrocyte sedimentation rate will be raised.
- Serum Creatinine
- Blood urea
- Bleeding Time
- Clotting Time
- Prothrombin Time

URINE ALUBUMIN, SUGAR , DEPOSITS:

This is to rule out renal pathology Albuminuria is more common in systemic lupus erythematosus patients.

IMMUNOLOGICAL TESTS;

Antinuclear antibodies are elevated in 95% of patients with systemic lupus erythematosus. However their absence does not rule out the diagnosis.

Anti Nuclear Antibodies can be seen in other systemic diseases. But antibodies to double stranded and anti smith antibodies to polypeptides that complex with certain species of nuclear RNA are quite specific for systemic lupus erythematosus. Disease activity in systemic lupus erythematosus can be correlated with high titres of Anti Nuclear Antibodies and low complement levels and with high titers of cryoglobulins by the Raji cell assay .Some of the antibodies found in systemic lupus erythematosus are as follows.

Specificity antigen	***clinical importance and comments***
Nuclear	multiple antigens detected: sensitive when Hep-2 or WIL-2 cells used; used quite non specific.
NativeDNA	highly specific for systemic lupus erythematosus seen in 70% of lupus patients, associated with nephritis and disease activity
Denatured DNA	high titers in systemic lupus erythematosus; low titers in other diseases
Sm (smith)	highly specific for systemic lupus erythematosus seen in 50% of patients

Histones	more common in drug induced systemic lupus erythematosus (95%)
Nuclear Ribonucleoprotein	seen in systemic lupus erythematosus highest titers in multiple connective tissue disease
Ro(SSa)	seen in primary sjogren syndrome and systemic lupus erythematosus
La(SSb)	seen in primary sjogren syndrome and systemic lupus erythematosus
Nucleolar	seen in scleroderma, primary sjogren and systemic lupus erythematosus
Phospholipid cardiolpin	seen in systemic lupus erythematosus and other diseases ;gives false positive VDRL
Clotting factors	lupus anticoagulants, cause prolonged PTT associated with venous and arterial thrombosis
Endothelial surface Antigens	may contribute to thrombosis

Platelet surface antigen	associated with thrombocytopenia
Erythrocyte surface antigens	occasionally associated with haemolysis
Lymphocyte surface antigens	may be associated with leucopenia and abnormal T cell function
Neuronal antigens	high titers are correlated with diffuse CNS Lupus

ELISA

Recent study using enzyme linked immunosorbent assay has shown that the level of plasma cell free Fc gamma receptor III (FcgammaRIII) also may increase significantly in patients with systemic lupus erythematosus. Also using ELISA, antibodies to human fibronectin (anti-fn) are detected in the sera of 34% of patients with systemic lupus erythematosus. There is an association with serum anti fibronectin antibodies and disease activity in systemic lupus erythematosus.

INTERLEUKINS

Soluble interleukin (IL-2)receptor (CD25) and soluble CD27 and CD 30 molecules are elevated in the serum of patients with systemic lupus erythematosus prior to an exacerbation of clinically evident disease activity. More over serum levels of interleukin-6 (IL-6) and interferon gamma have been found to be increased in patients with systemic lupus erythematosus.

Systemic lupus erythematosus patients may also show abnormality in their cerebrospinal fluid. There is local synthesis of oligoclonal IgG in 25% of cases and worsening of blood barrier function.

OCULAR INVESTIGATIONS

Clinical tests for dry eye

There is no single “gold standard” test for detecting dry eye disorders.

Schirmer I test is done without anaesthesia using Whatman filter paper ≠41. Room temperature and humidity must be consistent from test to test. The time of administration of the last drop and the time of testing are recorded. The test is done under ambient light conditions. Only one pair of tests should be done on a given day.

The test is done without touching the paper directly with the finger to avoid contamination of skin oil. The paper is placed at the junction of the middle and lateral one third of the lower eye lid. The patient is told to look forward and blink normally while a strip is placed in the right eye followed by the left eye. The strips are removed after 5 min and the amount of wetting is recorded in millimeters. The amount of wetting less than 10mm is considered to be positive.

Basal Schirmer test is done after anaesthetising with a drop of proparacaine. Schirmer strips are placed and the wetting is recorded. Amount of wetting less than 5mm is considered to be positive.

Augumented Schirmer test: Schirmer strips are placed and the nasal mucosa is irritated near the middle meatus with swab sticks. Reflex tearing is present in non-Sjogren's syndrome and absent in Sjogren syndrome.

Tear break up time

Break up time may measured invasively by using fluorescein (FBUT) or non-invasively using a keratometer or a xeroscope (NBUT). Fluorescein breakup time may not be reproducible and may not reliably reflect disease. Fluorescein strips are wet with a standardised drop of non-preserved saline solution and the strip is touched to the interior palpebral conjunctiva. Subjects are asked to blink several times and asked to move their eyes around thoroughly mix the fluorescein with the tear film. Patients are asked to first close and then open their eyes. The time from opening of the eyes to the appearance of the first dry spot is measured three times and the mean is recorded. A 10 second reference value is taken and <10 seconds is taken as abnormal.

Non invasive breakup time requires a keratometer or a xeroscope. Break up times are shorter using a keratometer as compared to xeroscope.

Rose Bengal staining

Rose Bengal stains areas of ocular surface where the tear film is discontinuous. It is commercially available as impregnated strips. Classically, the Van Bijsterveld grading system has been used assigning a grade (0-3) based on density of staining of the temporal and nasal conjunctiva and cornea of each eye.

Examination by light passed through green filter is recommended after Rose Bengal staining.

Tear film osmolarity

This test has high sensitivity and specificity when used as a single test and hence is taken as a “gold standard”. However, it is unable to distinguish evaporative and tear deficient dry eye. The technique requires determining osmolarity on basal tears and the avoidance of reflex tearing. Commercially osmometers are available. But the process still needs standardization and an experienced technician.

Other tests are:

Fluorescein clearance test

Lissamine Green staining

Tear ferning

Conjunctival impression cytology

Brush cytology

Lysozyme assay

Lactoferrin assay

Tear protein analysis

Slit Lamp examination

Indirect ophthalmoscope

Anterior chamber tap

Vitreous tap

Fundus fluorescein angiography

Aim: To evaluate retinal perfusion

To detect retinal neovascularsation

Confirm lupus choroidopathy

Findings:

- Areas of poor capillary bed perfusion usually around disc and macula[21]
- Abrupt termination of retinal arteries and arterioles
- Focal areas of capillary drop outs – cotton wool spot, irregular retinal vessel caliber

- Marked stasis with segmentation of blood column and dye extravasations in veins
- Neo vascular tufts seen as points of dye leakage

DIAGNOSIS

The diagnosis of systemic lupus erythematosus is based on a combination of clinical and laboratory criteria, which have varied over the past decade. Two of the most useful systems are those proposed by Cohen and associates (and accepted by the American Rheumatism Association) and by Hahn.

American rheumatism Association criteria

The revised 11 diagnostic criteria proposed by the American Rheumatism Association (ARA) are accepted widely. The diagnosis of SLE can be made if four of these criteria are met, serially or simultaneously, during any interval of observation. Ocular disorder is not one of the criteria.[20,26]

Criteria for classification of SLE

Criterion	Sensitivity (%)	Specificity (%)
Malar rash: flat or raised erythematosus rash over malar eminences	57	96
Discoid rash: raised, erythematosus patches with adherent keratoic scaling and follicular plugging	18	99

Photosensitivity: skin rash by history or physician observation caused by unusual reaction to sunlight	43	96
Oral or nasopharyngeal ulcers: usually painless	27	96
Nonerosive arthritis: involving two or more peripheral joints	86	37
Serositis: pleuritis (by history or if rub or effusion are present) or pericarditis (electrocardiographic changes, rub, or pericardial effusion)	56	86
Renal disorder: persistent proteinuria or cellular casts	51	94
Neurological disorder: seizures or psychosis in the absence of metabolic disease or offending drug	20	98
Hematological disorder:anemia, leucopenia, lymphopenia, or thrombocytopenia	59	89
Immunological disorder: positive lupus erythematosus cell preparation, anti-DNA antibodies, anti-Sm antibodies, or false-positive serology for syphilis	85	93
Antinuclear antibody: abnormal titer in the absence of known offending drugs	99	49

Hahn's criteria

Anti Nuclear Anti Bodies (1:5) + score of 7 points

	Points
Butterfly rash	2
Rash biopsy findings compatible with SLE	2
Polyarthritis	2
Serositis	2
Glomerulonephritis biopsy findings compatible with SLE	2
LE cells	2
Rash compatible with SLE, not biopsy-proved	1
Clinical nephritis, no biopsy	1
Organic brain syndrome	1
Localizing neurologic signs	1
Alopecia	1
Raynaud's phenomenon	1
Nail-bed capillary abnormality	1
Arthralgia	1
Fever	1
Retinal cytoid bodies	1

Polymyositis	1
Myocarditis	1
Hemolytic anemia	1
Leucopenia	1
Thrombocytopenia	1
Lymphadenopathy	1
Positive results on direct Coombs' test	1
False-positive STS results	1
Antibodies to DNA	1
Hypergammaglobulinemia	1
Hypocomplementuria	1
Circulating anticoagulant	1

TREATMENT

Therapy for the ocular surface manifestations of systemic lupus erythematosus is based on successful control of the underlying disease, as well as local therapy for the keratitis and tear deficiency. The usual therapy for sicca syndrome (tear replacement, soft contact lenses, punctal occlusion) may produce both symptomatic and objective improvement. Topical steroid therapy maybe a useful adjunct to systemic steroid therapy in the treatment of the scleritis. The retinopathy resolves only with successful control of the underlying systemic disease. Immunosuppression, primarily with corticosteroids, is the mainstay of therapy. Immunosuppressive drugs like cyclosporine A 2.5 mg to 5mg/kg/BW 2 times daily are also given. Other immunosuppressants used are tacrolimus, methotrexate, azathioprine and cyclophosphamide. Recently mycophenolate mofetil, which inhibits purine synthesis, has been tried.

Laser photocoagulation for proliferative retinopathy, using criteria from studies on diabetes and branch retinal vein occlusions, is believed to be beneficial. However, there is a report of a case of anterior segment ischemia in a patient after panretinal photocoagulation for proliferative lupus retinopathy. Although the mechanism of ischemia was unclear, the authors suggested avoiding undue pressure with the contact lens during laser photocoagulation,

keeping the treatment sessions short, and avoiding the use of retrobulbar anesthesia will help to prevent this complication. Flat retinal new vessels are treated by argon laser spots 200-500μm for 0.1 sec. Panretinal photocoagulation 500μm for 0.1 sec 1500-2000 burns in 2to 3 settings. Finally, surgical intervention may be necessary in patients with vitreous hemorrhage and tractional retinal detachment.

Systemic treatment

Many patients with systemic lupus erythematosus have relatively mild disease, and they will lead relatively normal lives with conservative therapy in the form of adequate rest and nutrition, use of a skin-protective sunscreen when avoidance of sun exposure is impossible, and use of salicylates and other nonsteroidal antiinflammatory agents for control of arthralgia, myalgia, low-grade serositis, and mild constitutional symptoms. Antimalarial therapy (e.g., hydroxychloroquine sulfate) may be the next step employed in arthralgia and arthritis control or in therapy for cutaneous lesions or mild anterior segment ocular inflammatory lesions if non-steroidal antiinflammatory agents have not been effective. One must be careful to watch for the possibility of development of a drug-induced retinopathy. Patients can test themselves with an Amsler grid.

Severe manifestations of systemic lupus erythematosus require therapy with systemic corticosteroids. Disabling constitutional symptoms and articular, cutaneous, and other systemic manifestations of the disease unresponsive to the

aforementioned conservative therapy should be treated with the minimum daily dose of corticosteroid required for adequate control of disease activity. Alternate-day steroid therapy is ineffective in the treatment of systemic lupus erythematosus, and most patients respond considerably better to divided daily doses (e.g., two or three times a day) than to single morning doses of corticosteroid. Severe disease affecting the central nervous, cardiovascular, pulmonary, or renal system may require initial high-dose (60-300 mg of prednisone/day) steroid therapy, tapered as soon as clinical improvement warrants it. In tapering daily prednisone dosage from the 60mg/day level, a useful rule of thumb is to decrease the dosage by 10 percent every 3 days until 40mg/day is reached; then the tapering should be slower.

Systemic lupus erythematosus renal or CNS crisis is usually treated with high-dose intravenous steroid therapy (1-2 gm of methylprednisolone/day for 3-6 days) in conjunction with high-dose oral steroid (100-300 mg of prednisone/day). Combination corticosteroid-cytotoxic therapy may be helpful in cases of severe systemic lupus erythematosus and in cases in which the systemic corticosteroids cannot be tapered below toxic levels without exacerbations of clinical disease. Cyclophosphamide may be the most effective cytotoxic agent studied for this purpose. Plasmapheresis for lupus crisis is also under investigation. Dapsone has yielded good therapeutic results in certain forms of systemic lupus erythematosus.

REVIEW OF LITERATURE

1. **Ophthalmic manifestations in Asian patients with systemic lupus erythematosus** Yap EY, Au Eong KG, Fong KY, Howe HS, Boey ML. Cheah WM Feng PH.

Singapore Med Journal, 1998 Dec; 39(12) : 557-9.

A study conducted on 70 Asian patients with systemic lupus erythematosus from tertiary rheumatology unit to ophthalmology Department.

70 patients were included in the study. There were 66 females (94%) and 4 males (6%) the mean age of patients was 32.9 yrs (9-67). 5 patients (7%) had ophthalmic symptoms while 65(93%) were asymptomatic. Eighty-three eyes of 45 patients had abnormal schrimers test. 27 of these eyes of 17 patients also had concomitant rose Bengal staining of the cornea and the conjunctiva. Seventeen eyes of 9 patients had retinal vascular lesions. Fourteen of these eyes had mild microangiopathic retinopathy with BCVA of 6/12 or better and 3 had retinal vaso occlusive disease with BCVA worse than 6/12. 28 eyes of 14 patients had cataract and 3 eyes of 2 patients had raised intraocular pressure. 12 eyes of 7 patients had BCVA worse than 6/12 because of optic neuropathy (4 eyes), Posterior subcapsular cataract (4 eyes), Retinal vaso occlusive disease (3 eyes) and phthisis bulibi (1 eye). None had any eyelid lesion, extraocular motility disorder or retrochiasmal disorder of vision.

2. Retinal Disease in patients with systemic lupus erythematosus

Osmau Ushiyama, Keiko Ushiyama Syuichi Koarada, Yoshifumi Tada Noriaki Suzuki Akihide Ohta, Shinji Oono Kohei Nagasawa.

Ann. Rheumatology Dis 2000; 59: 705-708.

A cross sectional study was made in 69 patients with systemic lupus erythematosus. The incidence retinopathy was young in 7/69 patients (ie) 10% of patients. The finding included vasculitis, cotton wool spots, hard exudates all which was considered to reflect vascular damage. The patients with retinopathy had higher levels of serum Creatinine than the patients without retinopathy ($p<0.01$).

3. Ocular manifestation of systemic lupus erythematosus in children.

A1 – Mayouf SM, Al – Hemidan AI.

Saudi Med J.2003 Sep; 24(9): (964-6).

52 consecutive children (45 females) with systemic lupus erythematosus completed evaluation. The mean ages of patients were 11.3 years. 18 patients (34.6%) had ocular manifestation seven patients had abnormal schrimers test (2 bilateral, 5 unilateral). Five patients (4 unilateral, one bilateral) had retinal vascular lesions. One patient had bilateral iridocyclitis. 3 patients had unilateral optic neuropathy and 11 patients had visual field defects (4 bilateral, 7 unilateral).

4. Neuro Ophthamological manifestations of systemic lupus erythematosus in Asian patients.

Teoh SC, Yap EY, Au Eong KG.

Clinic experiment ophthalmology 2001Aug: 29(4) 213-6.

To report 8 patients diagnosed as systemic lupus erythematosus who presented with a variety of neuro ophthamological complications. The most common manifestation was that of optic neuropathy and eye movement abnormalities. Ophthalmologist may need to consider the diagnosis of systemic lupus erythematosus in young woman who present with a recent onset of neuro ophthalmologic symptoms and signs.

5. Unusual eye manifestations in systemic lupus erythematosus patients.

Drosos AA, Petris CA, Petroutsos GM, Moutsopoulos HM.

Clinic Rheumatology 1989 Mar; 8(1): 49-53.

112 of patients with systemic lupus erythematosus were reviewed. 4 cases of unusual ocular manifestation are described. We found that anterior uveitis is not an uncommon manifestation of systemic lupus erythematosus and physician must be aware of it during patient evaluation since it can be treated without serious visual loss. Optic neuritis is uncommon in systemic lupus erythematosus and visual loss may be permanent despite therapy.

6. Systemic lupus erythematosus and the eye.

Quan Dong Nguyen, C. Stephen Foster.

IOC – Volu 38(1) 1998; Pg 33-36.

The diagnosis of systemic lupus erythematosus can be made if 4 of the 11 criteria by American Rheumatism Association are met, serially or simultaneously during any interval of observation. Ocular disorder is not one of the criteria. 90% of systemic lupus erythematosus patients are women with usual age of onset between the ages 15 and 45. The most common ocular manifestation of systemic lupus erythematosus, Keratoconjuctivitis sicca with or without xerostomia, Occurs in 25% patients. Retinal involvement in systemic lupus erythematosus is quite common second only to Keratoconjuctivitis sicca.

7. Prominent ocular findings as an early manifestation and of systemic lupus erythematosus.

Ashish. M.Mehta MD., Thomas E Frane M.D.

JPOS volume 35(2) 1998 Mar to Apr 114-115.

Unusual for ocular manifestation to precede with initial presentation of systemic disease. Gold and his colleagues showed 6.6% incidence of superficial keratitis and 1.6% uveitis (location unspecified).

8. Corneal staining in systemic lupus erythematosus

Spaeth GL:

N Eng J. Med 276 1186/1987

Spaeth in a study of systemic lupus erythematosus patients hospitalised at National Institute of ophthalmology stated that 88% had superficial punctate keratitis with fluorescein corneal stain. He reported that schrimer test were normal in some of these patients and therefore the issue of whether the superficial punctate keratitis seen in systemic lupus erythematosus is always truly the result of sicca syndrome or in fact due to corneal epithelial damage is unclear. Patient also exhibits punctate keratitis unrelated to dry eye status.

9. External ocular finding in lupus erythematosus: a clinical and immuno pathological study.

Peggy Frith, S M Burge, P R Millard, F Wonjnarowska

British Journal Ophthalmology 1990, 74, 163-167.

A selected group 18 patients with systemic lupus erythematosus were examined for dryness of eyes. It was found in 2 of 11 patients. The five patients had recurrent episcleritis. More than half of the patients had ocular manifestation. Ocular features can occur early and may be sufficiently characteristic to suggest the diagnosis of lupus erythematosus.

10. Retinopathy in systemic lupus erythematosus.

James Coppeto, Simmons Lessell.

Arch Ophthalmol- vol 95, May 1977. (797-799)

Reported 32 years old black women with systemic lupus erythematosus went rapidly blind due to severe bilateral Retinal vasculitis. The mechanisms appeared to be total arrest of retinal circulation by thrombosis of most retinal vessels including major arteries.

11. Optic Neuropathy in Systemic Lupus Erythematosus

Douglas A. Jabs, Neil R. Miller, Steven A. Newman.

Arch Ophthalmol 1986; 104: (564-568).

Reported 7 cases of optic neuropathy in systemic lupus erythematosus visual outcome varied, but improvement occasionally occurred following treatment with corticosteroids. The clinical picture was variable and could present as acute retrobulbar optic neuritis, ischemic optic neuropathy, or slowly progressive visual loss. All cases were due to vasco-occlusive disease in small vessels of the optic nerves.

AIM OF THE STUDY

- To determine the spectrum and prevalence of ocular manifestation of systemic lupus erythematosus.
- To identify potentially sight threatening lesions in ocular systemic lupus erythematosus.

MATERIALS AND METHODS

The study was carried out at Government Rajaji Hospital Madurai. A standardized ophthalmic examination on Madurai patients with systemic lupus erythematosus referred from the Dermatology Department and Rheumatology Department from Madurai were included in the study. The study was carried out prospectively and all ophthalmic examinations were carried out.

Relevant patient data recorded name, age, complaints, laboratory investigation reports including blood sugar, urea, serum creatinine urine albumin, total count, differential count, erythrocyte segmentation rate, bleeding time, clotting time, electrocardiogram, red blood cell count, Hemoglobin and Anti double stranded DNA results were recorded. Relevant ocular, family history and ocular complaints noted.

Ocular examination was carried in the routine manner using bright torch light using focal illumination, Binocular loupe and slit lamp examination was carried out for all cases.

The eyebrows, lids conjunctiva sclera, lacrimal system were closely studied. Tear film level, tear break up time, schrimer strip application, stained corneal examination was done in all cases. Tear film level of less than 0.3mm, tear break up time of less than 10seconds and schrimer strip less than 10mm were considered to be abnormal. Degree of dry eye status was noted. Cornea was checked for any opacities, punctate keratitis and interstitial keratitis.

Iris for any signs of iritis, iris atrophy, lens for any opacities were noted down. Corneal sensation was tested.

Visual acuity, intraocular pressure measurement using schiotz tonometer, fields by Bjerrum screen, recording was also done for all patients. Refraction and appropriate glass correction given. Fundus examination with a direct ophthalmoscope and indirect ophthalmoscope was done to rule out retinal central and peripheral lesions.

Retinopathy was defined as the presence of any of the following lesions; haemorrhages, vasculitis (Sheathing of retinal arterioles and /or venules or vascular tortuosity), cotton wool spots, papilloedema, optic atrophy, or retinal detachment according to the report of Stafford- Brady et al. In addition to these findings, we also included hard exudates unless the patients had essential

hypertension or diabetes mellitus, because they were considered to be the result of deposition of exudated lipids or proteins form the degenerated ocular nerves or from vessels with hyperpermeability. Retinal lesions considered to be caused by hypertension (that is, not caused by Systemic Lupus Erythematosus), arteriosclerosis, or diabetes mellitus, were excluded.

Renal disease was defined according to 1982 ACR criteria: persistent proteinuria (>0.5g/day or >3+) or cellular casts, or both. In addition, a raised serum creatinine level (normal >84μmol/l) was also included in the index. The data were analysed statistically by proportion test and Wilcoxon signed Rank Test.

All findings were entered in the proforma for further analysis.

OBSERVATIONS AND RESULTS

Total No: of Patients – 33

Total No: of eyes examined – 66.

During this period of study from January 2004 to January 2006, the total Number of systemic lupus erythematosus patients reported to Ophthalmology Department was 33. The total No: of females were 31 and there were 2 males.

1. Age Distribution

Table 1

Age	No of patients	Percentage
1-10	0	-
11-20	7	21.2%
21-30	18	54.55%
31-40	7	21.2%
Above 40	1	9.09%

The youngest female reported was 11 years of age.

Out of 33 patients examined 7(21.2%) patients were in the age group of 1-20 years and 18(54.55%) patients were in the age group of 21-30 years and 7(21.2%) patients were in the age group 30-40 years. One case of above forty years of age was reported in this study.

2. Sex distribution:

Table 2

	No .of Patients	**No. of Percentage**	**Comparative Study**
Males	2	6.06%	6%
Females	31	93.9%	94%

In this study 31(93.9%) patients were females and 2(6.06%) patients were males.

3. Ocular Manifestation in Systemic lupus erythematosus

Table 3

Ocular Manifestation	**No of Patients**	**Percentage**
Present	21	63.63%
Absent	12	36.36%

Out of 33 patients in study group, 21(63.63%) patients had some manifestation in the eyes where as 12(36.36%) patients had no manifestation. Their ocular examination was normal.

4. Ocular Symptoms in Systemic lupus erythematosus

Table 4

Symptoms	No of Patients	Percentage
Symptomatic	3	9.09%
Asymptomatic	30	90.9%

Out of 33 patients only 3(9.09%) patients complained of ocular symptoms. 2 patients had complaints of decreased vision and irritation and one patient complained of floaters. The rest 30 (90.9%) patients were asymptomatic.

5. Abnormal Schrimer's and Systemic lupus erythematosus:

Table 5

Schrimer's test	No of Patients	Percentage
Abnormal	9	27.27%
Normal	24	72.73%

Out of 33 patients 9(27.27%) patients. (6 Bilateral and 3 unilateral) had abnormal schrimer test. Associated changes of tear film level, tear break up time were also seen. 27.27% of patients had abnormal schrimer test.

Various studies showing abnormal schrimer :

Various studies showing abnormal schrimer in systemic lupus erythematosus are tabulated

TABLE 6

Studies	Percentage
YAP EY & others	64.2%
Peggy Frith	22%
Steinberg Ad et al	25%
Present Study	27.27%
AlMayouf SM et al	13%

6. Keratitis and Systemic lupus erythematosus:

TABLE 7

Keratitis	No of Patients	Percentage
Present	4	12.12
Absent	29	87.88

4 (12.2%) patients of keratitis were found out of 33 patients. All the 4 patients had punctate superficial epithelial erosion. All the 4 patients had inferior superficial punctate epithelial erosion. No case of interstitial keratitis and peripheral ulcerative keratitis were reported.

7. Comparison of keratitis and abnormal schrimer

TABLE 8

Keratitis	Schrimer test	
	Normal	Abnormal
Absent	23	6
Present	1	3

All keratitis were in the inferior part of cornea. Out of the 4 cases of keratitis, 3 patients had abnormal schrimer and one had normal schrimer. Out of 23 patients who had normal schrimer only one case of keratitis was reported.

8.Uveitis and Systemic lupus erythematosus

Table 9

Uveitis	No of Patients	Percentage
Present	1	3.03
Absent	32	96.97

Uveitis is seen only in one(3.03%) patient which resolved with steroids. Patients presented with keratic precipitates, flare, cells with fibrinous membrane at pupillary margin unilaterally.

9. Visual acuity and Systemic lupus erythematosus :

TABLE 10

Visual acuity	No of Patients	Percentage
6/12 – PL	4	12.12
6/6 – 6/12	29	87.88

7 eyes of 4(12.12%) patients had visual acuity of less than 6/12. Posterior subcapsular cataract was found in 6 eyes of 3 patients. Visual acuity was diminished in 2 eyes due to optic neuritis and in 4 eyes due to retinal vasculitis. One patients had episcleritis with refractive error.

10. Intraocular pressure, orbit and adnexa:

Tension was normal in all cases. No orbit and adnexal pathology were found in our study.

11. Optic neuritis and Systemic lupus erythematosus

TABLE 11

Optic neuritis	No of Patients	Percentage
Present	1	3.03
Absent	32	96.97

Various studies of optic neuropathy and systemic lupus erythematosus

TABLE 12

Studies	Years	No of patients	Clinical Presentation
Vitale et al,	1973	2	Optic neuritis
Hackett et al,	1974	3	Optic neuritis
Shepherd et al,	1974	2	Retrobulbar neuritis
Kenkre et al,	1978	1	Optic neuritis
Kinney et al,	1979	1	Optic atropy
Allen et al	1979	1	Retrobulbar neuritis
Lessel et al	1979	2	Optic neuritis
		1	Retrobulbar neuritis
Smith et al	1982	2	Optic neuritis
		1	Retrobulbar neuritis
		1	Optic atropy

12. Retinal vasculitis and **Systemic lupus erythematosus**

TABLE 13

Patients	Retinal haemorrhage	Vasculitis	Cotton wool spot	Hard exudate
1		1		
2	1	1	1	
3.	1	1		
4.	1			1

4 patients had retinal vasculitis compared to 29 patients without changes. The incidence of retinal vasculitis is 12.2%. Vasculitis indicates vessel sheathing/ vessel narrowing/ tortusity. 3 patients had retinal haemorrhage, 3 patients had vasculitis. Cotton wool spot and hard exudates were found in one patient.

13. Comparison of Retinal vasculitis and Renal disease:

TABLE 14

Renal disease	Retinal vasculitis	
	Present	Absent
Present	3	7
Absent	1	22

Out of 10 patients who had renal disease according to ACR criteria 3 patients had vasculitis compared to 7 patients without vasculitis. One patient had retinal vasculitis without renal disease where as the other 22 patients were normal.

14. Comparison of Asian study & present study

TABLE 15

Parameters	**Asian study**		**Present study**	
	Patients	**Percentage**	**Patients**	**Percentage**
Total no of patients	70	-	33	-
Males	4	6	2	6.06
Females	66	94	31	93.9
Mean age	32.9	-	27.20	-
Symptomatic patients	5	7	3	9.09
Ocular manifestation	-	-	21	63.63
Abnormal schrimer	17	64.2	9	27.27
Retinal vasculitis	9	12.85	4	12.12
BCVA < 6/12	7	10	4	12.12
Tension	2	2.8	-	-
Uveitis	-	-	1	3.03
Keratitis	-	-	4	12.12

DISCUSSION

This study was conducted in Government Rajaji Hospital during the period January 2004- 2006. 33 patients who were diagnosed as systemic lupus erythematosus by ARA criteria were analysed for ocular manifestation.

The youngest female reported was 11 years of age and oldest female was above 45 years. Out of 33 patients 21.2% were in the age group of 11- 20 years and 54.5% were in the age group of 21-30 years. 21.2% were in the age group of 30-40 years.

According to Quan Dong Nguyen and C. Stephen foster in his study, "Systemic lupus erythematosus and Eye" has stated, "90% of systemic lupus erythematosus patients are woman with usual age of onset between the ages 15-45 years". In this study, only 2 patients were under 15 years 1 patient were over 40 years. Most of the patients (93.94%) were in the age group of 15-45 years. Applying statistical analysis by proportion test it was inferred that age factor does not influence ocular manifestation. (i.e) Incidence of abnormal ocular manifestation is not due to age factor ($p > 0.05$)

There were 31 females and 2 males in this study. This result was similar to the study by YAPEY, Au Eong KG Fong KY, Howe HS, Boev ML, Cheah WM, Feng PH were they have quoted and incidence of 94% females and 4%

males. Hence systemic lupus erythematosus is common in female of child bearing age group (15-45) years.

Ocular manifestations were found in 63.63% of study group. This stresses the importance of ocular manifestation in systemic lupus erythematosus. In the study by Peggy Frith and coworkers they have stated, “overall nearly half the patients had signs which could have been related to the underlying systemic lupus erythematosus. In a study done in children (ie) Ocular manifestation of systemic lupus erythematosus in children by Al-Mayouf SM, Al-Hemidam A1. They have quoted an incidence of 34.6%(18patients). Compared with children adults have higher incidence of manifestation.

Out of 33 patients only 3(9.09%) patients complained of ocular symptoms. 2 patients had complaints of decreased vision and irritation and one patient complained of floaters. The rest 30 (90.9%) patients were asymptomatic. In the study Peggy Frith, “twelve patients or two-thirds, reported ocular symptoms. Intermittent redness of one or both globes with moderate discomfort and no discharge was suggestive of recurrent episcleritis some had itching and remaining were asymptomatic. Present studies incidence correlated well with the study in Tang Tock Sen hospital by YAPEY, Au Eong KG Fong KY, Howe HS, Boev ML, Cheah WM, Feng PH in which 7% of patients were symptomatic on examination.

27.27% of patients had abnormal schrimer test. In the study by Tan Tock Sen hospital by YAPEY, Au Eong KG Fong KY, Howe HS, Boev ML, Cheah WM, Feng PH, out of 70 patients 45 patients had abnormal schrimer test. This accounted for 64.2%. Where as the incidence of abnormal schrimer in the study by Al Mayouf SM , AL Hemidan AI, was found to be13%.

In a study by Peggy Firth, “External ocular finding in lupus erythematosus” the incidence of dry eye was 2 out of 11 patients and it accounted for 22%. Lastly the study by Steinberg AD et al, has quoted that “the most common ocular manifestation of systemic lupus erythematosus is keratoconjunctivitis sicca, approximately in 25% of patients.

Thus the incidence of abnormal schirmer and dry eye status varied in different studies. Probably the inclusion criteria for dry eye status and test reliability will account for the varied presentation.

4 (12.2%) patients of keratitis were found out of 33 patients. All the 4 patients had punctate superficial epithelial erosion. All the 4 patients had inferior superficial punctate epithelial erosion. No case of interstitial keratitis and peripheral ulcerative keratitis were reported.

Gold and his collegues have reported an 6.6% incidence of keratitis in systemic lupus erythematosus patients. Speath found in a study of systemic lupus erythematosus patients that 88% had superficial punctate kertatitis with

fluorescein corneal staining. Schrimer test results were normal in these patients, and therefore the issues of whether the superficial punctate keratitis seen in patients with systemic lupus erythematosus is a always truly the result of sicca syndrome or in fact is secondary to corneal epithelial damage associated with lupus disease activity is unclear.

In our present study, out of the 4 cases of keratitis, 3 patients had abnormal schrimer and one had normal schrimer. Out of 23 patients who had normal schrimer, only one case of keratitis was reported. Statistical analysis using proportion test infers that the incidence of abnormal schrimer is not related to the incidence of keratitis at 5% level of significance (ie) patient also exhibit punctate keratitis unrelated to dry eye status.

Uveitis is seen only in one (3.03%) patient, which resolved with steroids. Patients presented with keratic precipitates, flare, cells with fibrinous membrane at pupillary margin unilaterally. Reviewing the literature, one case of bilateral iridocyclitis reported by Al Mayouf SM, AL Hemidan in study “ocular manifestation of systemic lupus erythematosus in children”.

In the study by Drosos AA, Petris CA, Petroutsos GM, Moutsopoulos HM, “Unusual eye manifestations in systemic lupus erythematosus patients”, they have stated that anterior uveitis is not an uncommon manifestation of systemic lupus erythematosus and physicians must be aware of it during the

patient’s evaluation, since it can be treated without serious visual loss. Our case responded well with steroid and visual acuity improved.

Visual acuity in systemic lupus erythematosus patients were generally good but only 4 patients had less than 6/12 Best Corrected Visual Acuity. Out of these 4, 3 patients had posterior subcapsular cataract and one had optic neuritis. Many patients had refractive errors.

In the study by YAP EY and his collegues. Only seven patients had BCVA worse than 6/12 because of optic neuropathy (4eyes), posterior subcapsular cataract (4 eyes), retinal vasculitis (3 eyes) and one eye had Pthsis bulbi. Hence many patients had good visual acuity except for a few. He attributes post subcapsular cataract as a part of treatment sequalae for the patients who are on steroids. Yet vision-threatening complications can occur in systemic lupus erythematosus is well proven which if intervened at appropriate time will prevent serious visual loss.

Tension was normal in all cases in our study. 3 eyes of 2patients had raised intraocular tension in the study by YAPEY and his collegues. None had any orbit, eyelid lesion, extraocular modality disorder or a retrochiasmal disorder of vision.

One patient had manifestation of disc edema with haemorrhage and vitreous opacities, diagnosed as optic neuritis. The visual acuity was 6/36 p.

The incidence of optic neuritis was found to be 3.03% in our study. Al Mayouf SM, AL Hemidan, has quoted incidence of 5.7% of optic neuritis in children.

Teoch SC, in a study “Neuro- ophthalmological manifestations of systemic lupus erythematosus in Asian patients” has stated that the most common manifestations were that of optic neuropathy and eye movement abnormalities. The outcome was variable ranging from complete recovery to optic atrophy with navigational visual acuity. Treatment was often empirical, although early treatment with corticosteroids has been tried with varying success.

Thus it is clear form our cases, as well as form those in the literature, that, although optic neuropathy in systemic lupus erythematosus is caused by an ischemic process in virtually all instances, the clinical presentation is quite varied. It would thus appear that in virtually any patient, particularly young women, who develop any type of optic neuropathy, whether unilateral or bilateral, the possibility of systemic lupus erythematosus must be considered, and an appropriate history, examination, and serologic studies may be required.

4 patients had retinal vasculitis compared to 29 patients without changes. The incidence of retinal vasculitis is 12.2%. Vasculitis indicates vessel sheathing/ vessel narrowing/ tortuosity. 3 patients had retinal haemorrhage, 3 patients had vasculitis. Cotton wool spot and hard exudates were found in one patient.

Retinopathy is one of the important, if not major, manifestation of systemic lupus erythematosus which develops with an incidence of 7%-26%. All the findings of retinopathy were considered to reflect vascular damage, such as vasculitis and thromboembolism. For instance, haemorrhages, which were seen in 3 patients, might have been caused by vasculitis, thromboembolism or hypertension. Vasculitis or microembolism of the vessel walls or neural fibres, or both, resulting in the formation of cotton wool spots and hard exudates. An important finding characteristic of lupus retinopathy is thought to be vasculitis of the retinal capillaries associated with local microinfarction. Charles describes the diagnosis of retinal vasculitis with perivascular exudates and patches of fluorescein leakage along vessels. Histological evidence of immune mediated vasculitis has also been reported in lupus retinopathy. On the other hand, ocular fundus is the only part of the human body where we can directly observe small vessels without injuring the tissue. This suggests that fundus examination should be carried out more often.

The retinopathy in patients with systemic lupus erythematosus was associated with renal dysfunction, CNS lupus, all of which were more or less related to vascular disorders. By applying statistical test (proportion test) in our study an inference has been made that the levels of abnormal Creatinine influences the changes in retinopathy in systemic lupus erythematosus.

[$p<0.01$]. Lupus retinopathy may reflect systemic vascular damage, which may develop in association with vasculitis.

Comparing Asian study and present study, all parameters were of the same incidence except the abnormal schrimer. It has been inferred by using Wilcoxon signed Rank Test that Asian studies and the present studies yield the similar results at 5% level of significance. Thus there is no racial discrimination in ocular manifestations.

SUMMARY

This clinical study was done at Department of ophthalmology Govt. Rajaji Hospital Madurai.

- A total of 33 patients were examined and out of which 31 (93.9%) were females and 2 (6.06%) were males.
- The mean age of manifestation of systemic lupus erythematosus were found to be range from 11 to 45 yrs – [27.20 yrs]
- Ocular manifestations were found in 63.63 % of patients in systemic lupus erythematosus.
- 3 patients (9.09%) were symptomatic on examination.
- 9 (27.27%) patients had features of dry eye (abnormal schrimer, less than 10mm, tear break up time less than (10sec)
- 4 patients (12.12%) had punctate epithelial keratitis
- Patients also exhibit punctate keratitis unrelated to dry eye status.
- One patient (3.03%) had unilateral anterior uveitis.
- 7 patients had worse than 6/12 Visual acuity (3 patients) Subcapsular cataracts, 2patients retinal vasculitis, 1 Optic neuritis, 1 episcleritis with refractive error.
- Intraocular pressure was normal in all cases.
- No eyelid lesion, orbital lesions were found

- One patient (3.03%) had optic neuritis
- Four patients (12.12%) had retinal vasculitis.
- The patient with retinal vasculitis had higher levels of serum creatinine than patients without retinal vasculitis.

CONCLUSION

Eye is a highly sensitive Barometer for the onset and reactivation of autoimmune phenomenon.

In this study the prevalence of ocular manifestation in systemic lupus erythematosus was 63.63%. This stresses the importance of ocular manifestation in systemic lupus erythematosus. Sight threatening complication can occur in systemic lupus erythematosus which if intervened at appropriate time will prevent serious visual loss. Patients with retinopathy in systemic lupus erythematosus had higher serum creatinine levels than patients without retinopathy.

Hence from these observations, ocular manifestation in systemic lupus erythematosus had led us to the belief that ocular inflammation should be added to the criteria for classification of systemic lupus erythematosus. Such inclusion may lead to better awareness of systemic lupus erythematosus ocular disease for the physician & may yield better outcome in diagnostic prognostic therapeutic ways for the patient.

PROFORMA

I. PATIENTS RECORD

Name Age Sex Male /Female:

Address I.P/O.P – No

II. Complaint:

Laterality Right eye Left eye Both eye

Symptoms: Defective vision

Foreign body sensation/ Irritation

Pain

Floaters

Duration

Onset

Severity

Course

Previous attack

SYSTEMIC HISTORY

General Fever/malaise / Loss of Weight/Loss of Appetite

Skin Rashes / nodules / utricaria / edema / raynaud phenomenon/ alopecia / ulcers

Joints Arthritis / Arthralgia

Neurological	headache / seizures / psychoses
Renal	edema of legs / puffiness of face / polyuria / oliguria

H/O INTAKE OF DURGS

Treatment history	On steroid
	Not on steroid
	Anti metabolites

OCULAR EXAMINATION

1. Eye brows	Madrosis
2. Eye lids	Madrosis
	Discoid lupus
3. Tear film	Tear film height/Tear break up time/
	Schrimer test
4. Conjunctiva	Congestion / pterygium / nodule
5. Cornea	keratitis (superficial punctate keratitis /ulcer/
	interstitial keratitis)
6. Corneal sensation	present / absent
7. Anterior chamber	shallow/ Normal depth / flare / cells
8. Iris	Iridocyclitis (Acute /chronic)
	synechiae
	membrane

9. Pupil size / shape /

reaction direct

Indirect

Relative afferent pupillary defect

10. Lens Clear

Immature cataract

Posterior sub capsular cataract

Mature cataract

Aphakia

Intra Ocular Lens

11. Best corrected Visual Acuity Right Eye

Left Eye

12. Staining of cornea

13. Intra Ocular Pressure

14. Fields

15. Colour Vision

16. Refraction Objective

Subjective

17. Fundus

Direct ophthalmoscope

Indirect ophthalmoscope

19. Orbit and adnexa

Diagnosis

Lab investigations

1. Total Count

   Differential Count

   Erythrocyte Sedimentation Rate

2. Urine Albumin

   Sugar

   Deposits

3. Haemoglobulin

   Red Blood Cell Count

   Platelets Count

   Bleeding Time / Clotting Time

4. Serum Creatinine

   Blood Urea

   Urine Protein

5. Peripheral Smear
6. Anti double stranded DNA
7. (LE) Cell

Treatment

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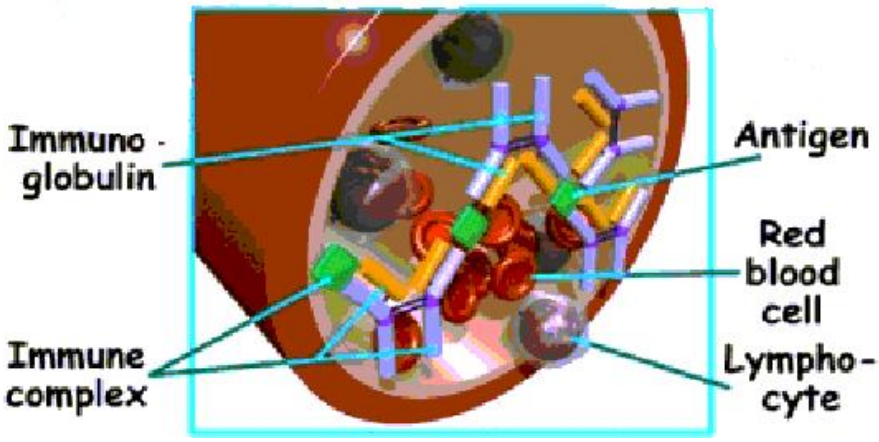
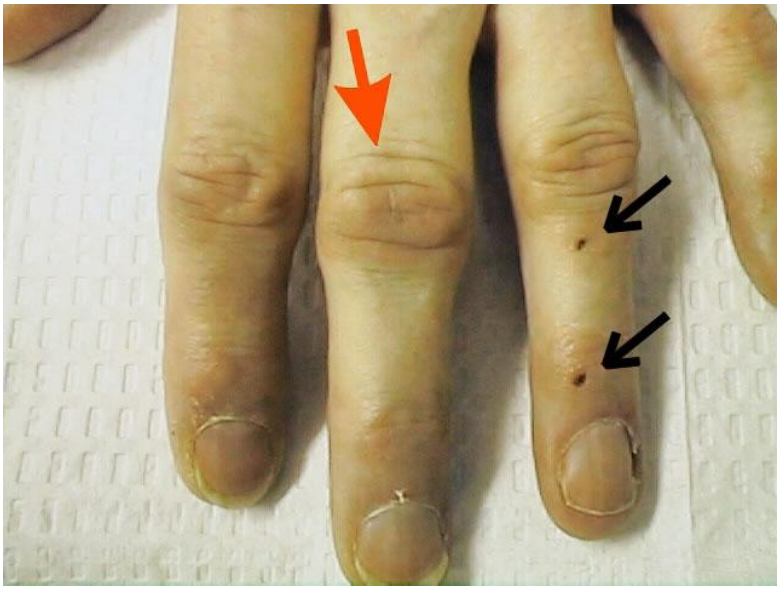
MACULOPAPULAR RASH WITH MUCOSAL ULCERATIONS

PATHOGENESIS

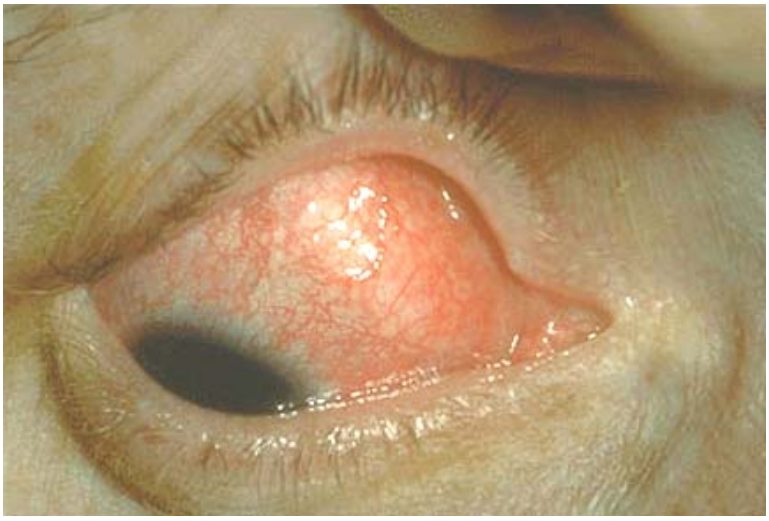


THE THICK RED ARROW DEMONSTRATES SYNOVIAL THICKENING AND SUBCUTANEOUS ERYTHEMA IN A PATIENT WITH SLE. THE THIN BLACK AREAS SHOW TWO SMALL SUBCUTANEOUS INFARCTS.



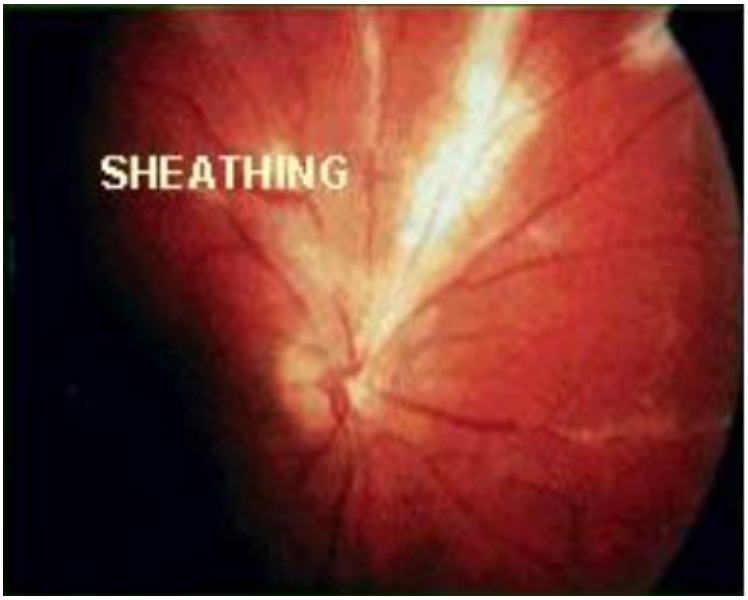
EPISCLERITIS

SCLERITIS

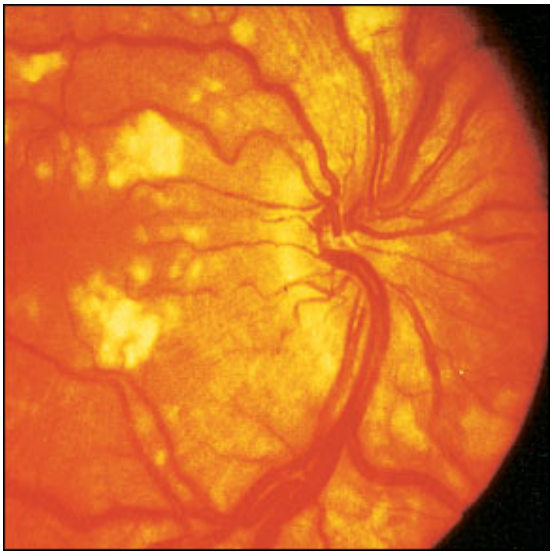


UVEITIS – POSTERIOR SYNECHIAE WITH FESTOONED PUPIL

RETINAL VESSEL SHEATHING



DISC EDEMA WITH MULTIPLE COTTON WOOL SPOTS



FUNDUS FLUORESCEIN ANGIOGRAPHY DYE LEAKAGE SEEN

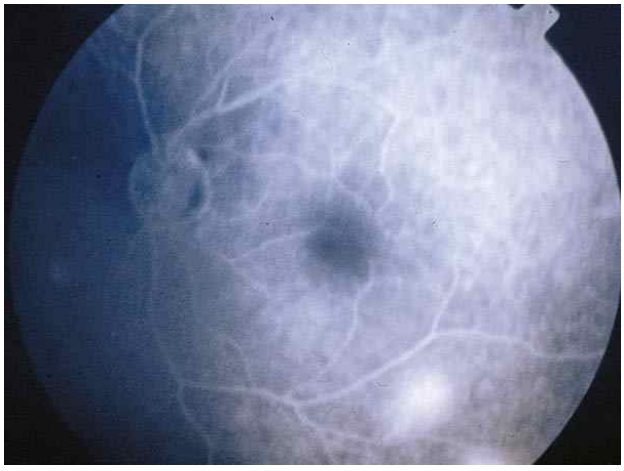


FIGURE -1

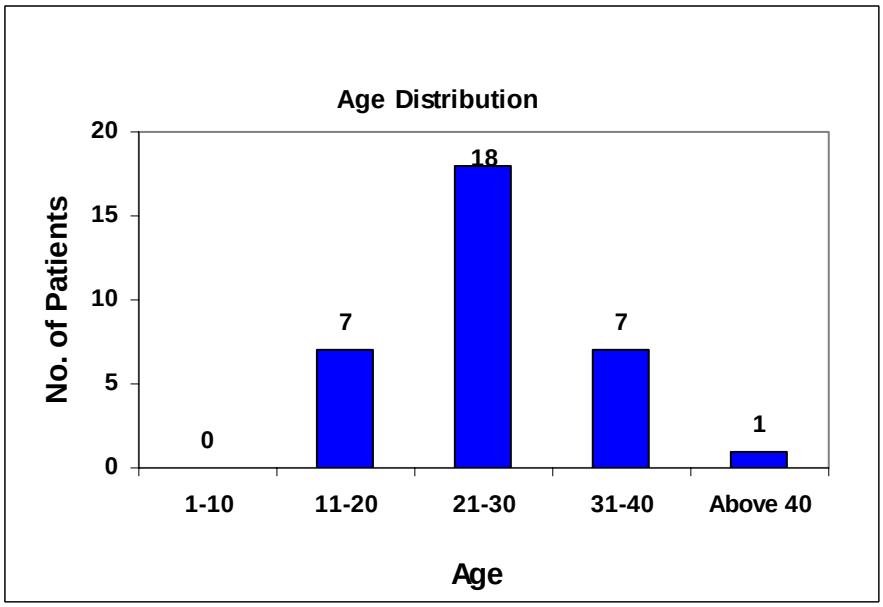


FIGURE -2

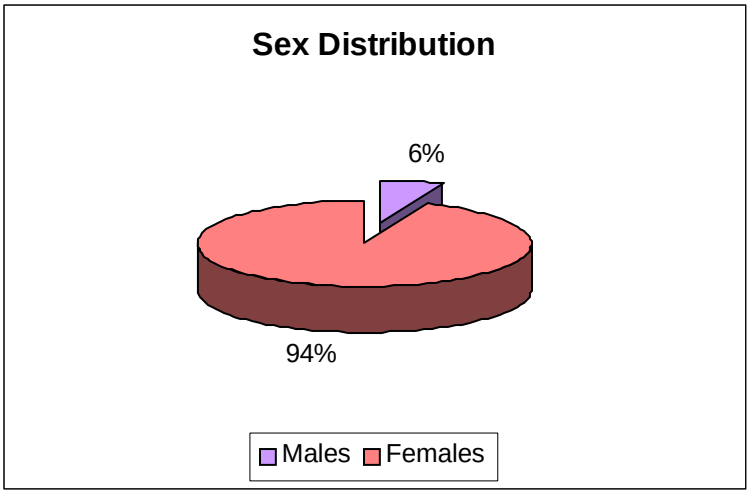


FIGURE -3

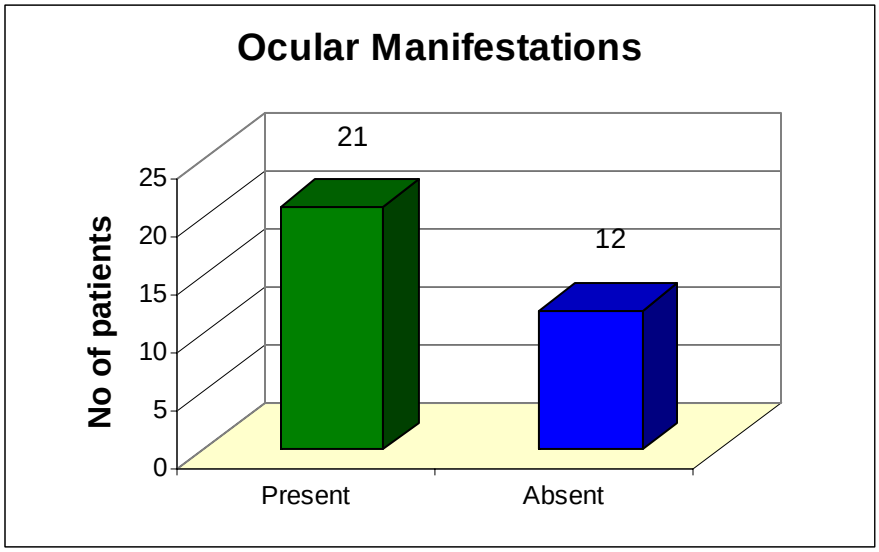


FIGURE -4

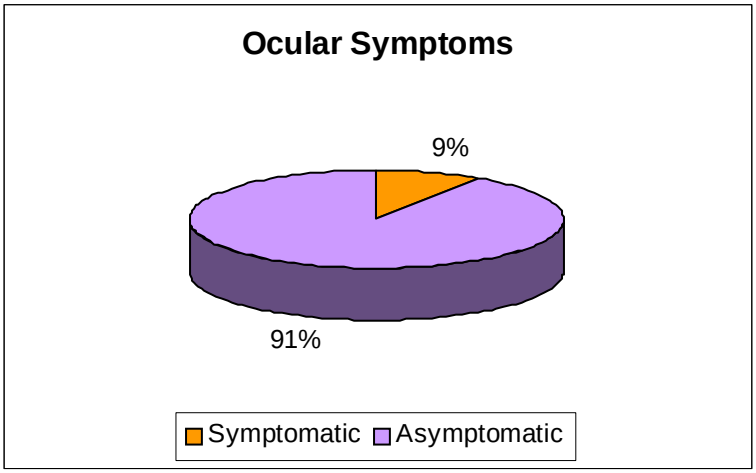


FIGURE -5

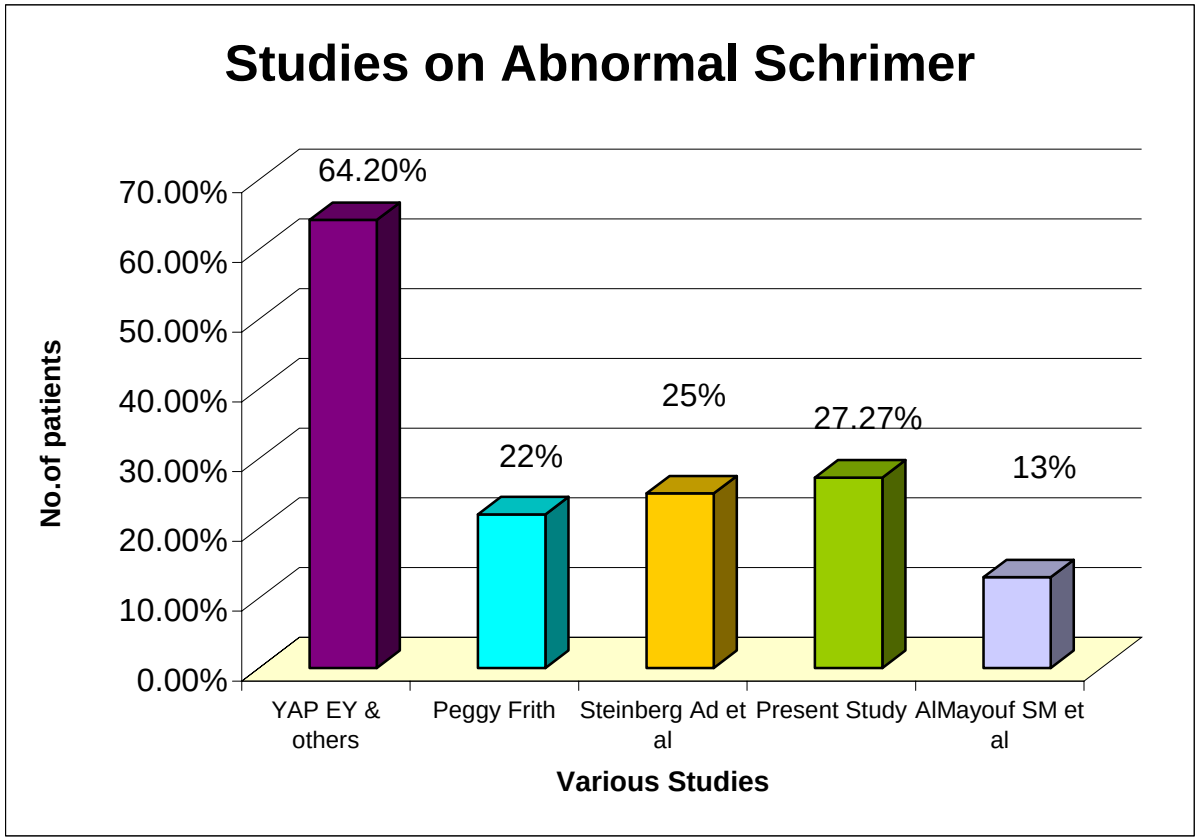

Studies on Abnormal Schrimer
No.of patients
70.00%
60.00%
50.00%
40.00%
30.00%
20.00%
10.00%
0.00%
64.20%
22%
25%
27.27%
13%
YAP EY & others
Peggy Frith
Steinberg Ad et al
Present Study
AlMayouf SM et al
Various Studies

FIGURE -6

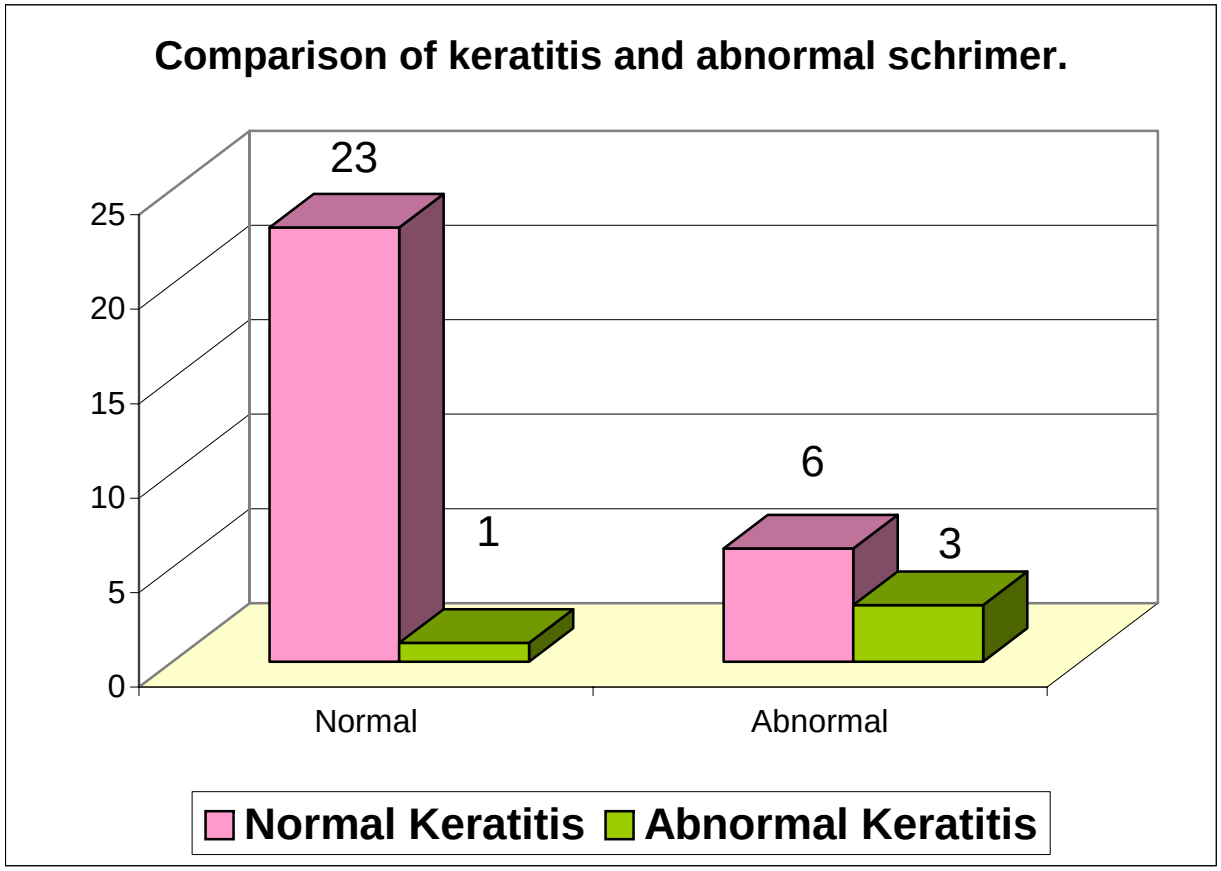

Comparison of keratitis and abnormal schrimer.
25
20
15
10
5
0
23
1
6
3
Normal
Abnormal
Normal Keratitis
Abnormal Keratitis

FIGURE -7

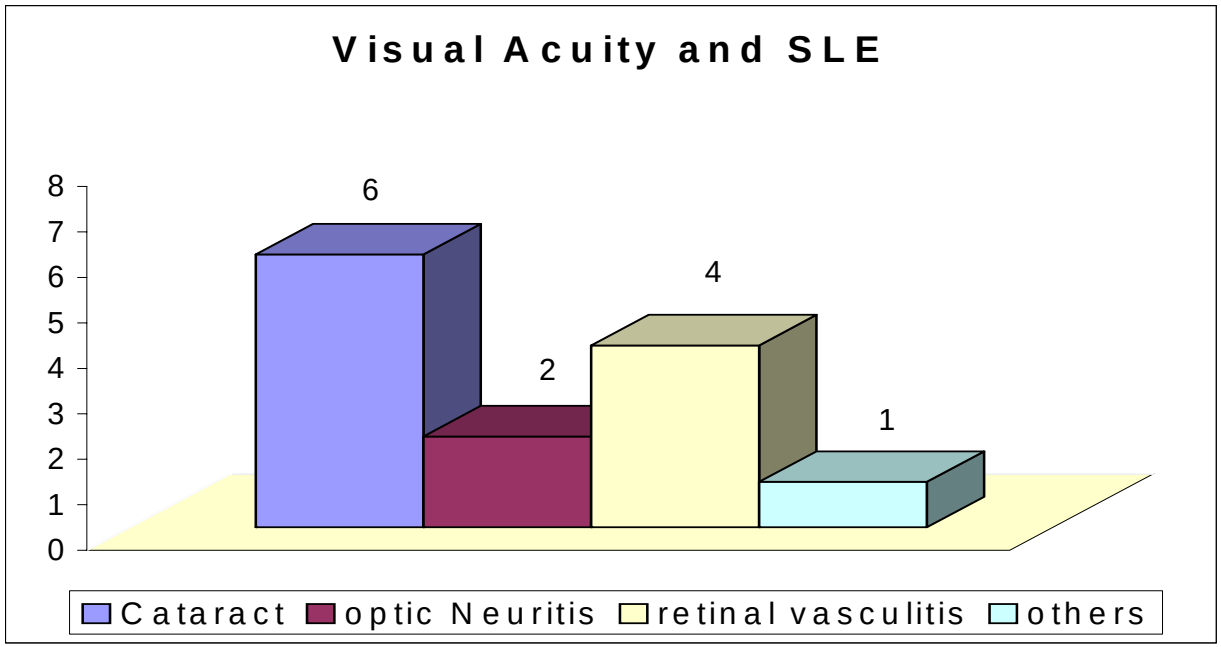
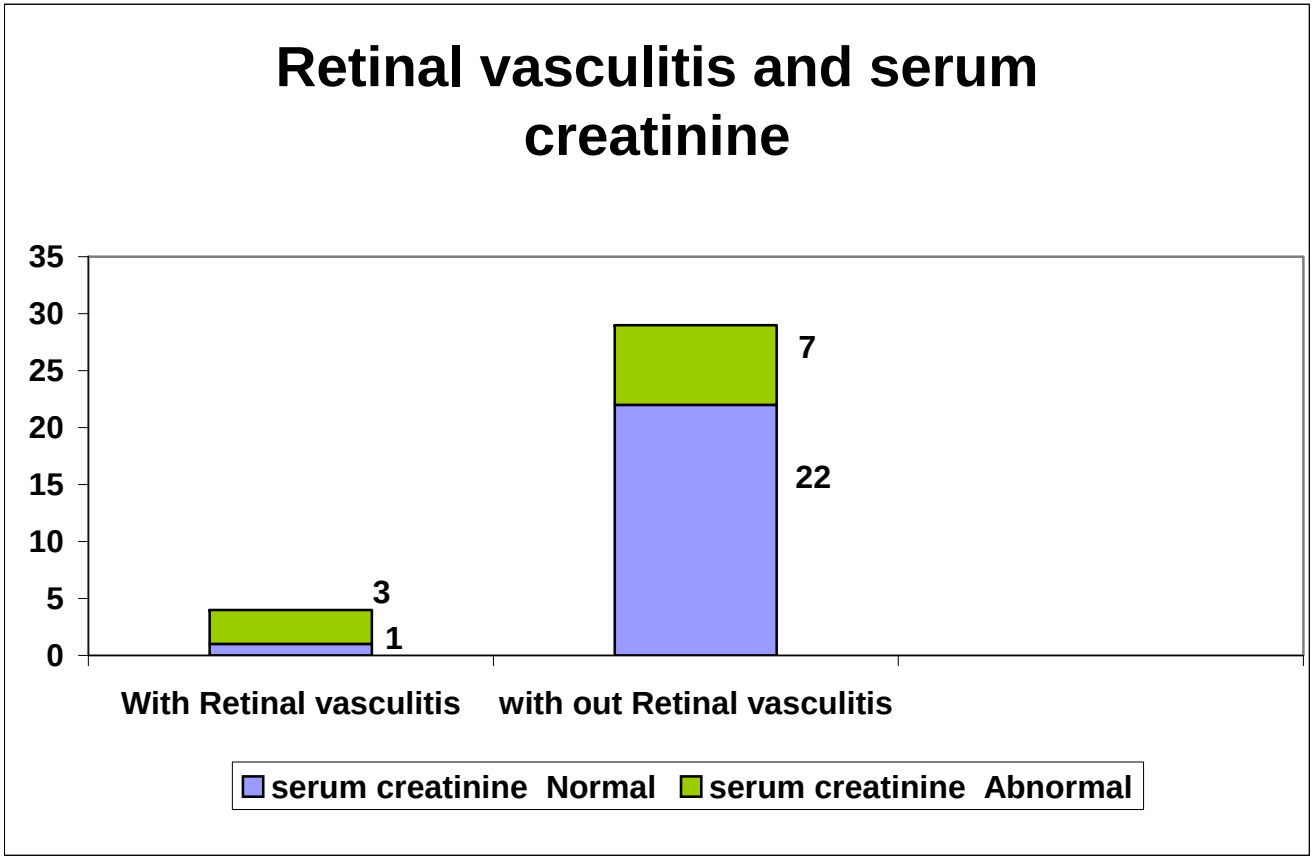

Visual Acuity and SLE
8
7
6
5
4
3
2
1
0
6
2
4
1
Cataract
optic Neuritis
retinal vasculitis
others

FIGURE -8


Retinal vasculitis and serum creatinine
35
30
25
20
15
10
5
0
3
1
7
22
With Retinal vasculitis
with out Retinal vasculitis
serum creatinine Normal
serum creatinine Abnormal

MASTER CHART CONTINUED

Serial No.	Name	Age	Sex	Ocular Manifestation	Symptoms	Renal Disease	Eye	Eyebrows/Lids	Conjunctiva	Tear Film level	Break up Time	Schrimer's Strip	Sclera	Cornea	Anterior Chamber	Iris	Pupil	Lens	Visual Acuity	Tension	Fields/Colou vision	Refractive Error	Orbit+Adnexa	Fundus				
																								Vitreous	Disc	Vessels	Macula	Background retina
							OD	1	1	2	2	2	1	1	1	1	1a	1	6/12	1	1	2	1	1	1	1	1	1
18	Sakira	25	F	2	1	1	OS	1	1	2	2	2	1	1	1	1	1a	1	6/6	1	1	1	1	1	1	1	1	1
							OD	1	1	1	1	1	1	1	1	1	1a	1	6/6	1	1	1	1	1	1	1	1	1
19	Alamelu	26	F	1	1	1	OS	1	1	1	1	1	1	1	1	1	1a	1	6/6	1	1	1	1	1	1	1	1	1
							OD	1	1	1	1	1	1	1	1	1	1a	1	6/6	1	1	1	1	1	1	2	1	1
20	Rathamala	29	F	2	1	1	OS	1	1	1	1	1	1	1	1	1	1a	1	6/9	1	1	2	1	1	1	2	1	1
							OD	1	1	1	1	1	1	1	1	1	1a	1	6/12	1	1	1	1	1	1	1	1	1
21	Chitra	14	F	1	1	1	OS	1	1	1	1	1	1	1	1	1	1a	1	6/12	1	1	1	1	1	1	1	1	1
							OD	1	1	1	1	1	1	1	1	1	1a	2	6/24	1	1	2	1	1	1	1	1	1
22	Prema	30	F	1	1	2	OS	1	1	1	1	1	1	1	1	1	1a	2	6/24	1	1	2	1	1	1	1	1	1
							OD	1	2	2	2	2	1	1	1	1	1a	1	6/9	1	1	1	1	1	1	1	1	1
23	Nagashar	23	F	2	1	1	OS	1	1	1	1	1	1	1	1	1	1a	1	6/12	1	1	1	1	1	1	1	1	1
							OD	1	1	1	1	1	1	1	1	1	1a	2	6/24	1	1	2	1	1	1	2	2	3
24	Anbuselvi	40	F	2	2	2	OS	1	1	1	1	1	1	1	1	1	1a	2	6/36	1	1	2	1	1	1	2	2	3
							OD	1	1	1	1	1	1	1	1	1	1a	2	6/12	1	1	2	1	1	1	1	1	1
25	Kanchana	38	F	1	1	2	OS	1	1	1	1	1	1	1	1	1	1a	2	6/9	1	1	2	1	1	1	1	1	1
							OD	1	2	2	2	2	2	2	1	1	1a	1	6/12	1	1	2	1	1	1	1	1	1
26	Devi	25	F	2	1	1	OS	1	2	2	2	2	1	2	1	1	1a	1	6/12	1	1	2	1	1	1	1	1	1
							OD	1	1	1	1	1	1	1	1	1	1a	1	6/6	1	1	1	1	1	1	2	1	1
27	Muthulaxmi	28	F	2	1	2	OS	1	1	1	1	1	1	1	1	1	1a	1	6/6	1	1	1	1	1	1	2	1	1
							OD	1	1	2	2	2	1	1	1	1	1a	1	6/6	1	1	1	1	1	1	1	1	1
28	Manjula	27	F	2	1	1	OS	1	1	2	2	2	1	1	1	1	1a	1	6/6	1	1	1	1	1	1	1	1	1
							OD	2	1	1	1	1	2	1	1	1	1a	1	6/9	1	1	2	1	1	1	1	1	1
29	Vanitha	20	F	2	1	1	OS	2	1	1	1	1	2	1	1	1	1a	1	6/9	1	1	2	1	1	1	1	1	1
							OD	1	1	1	1	1	1	1	1	1	1a	1	6/6	1	1	1	1	1	1	1	1	1
30	Femnia	22	F	1	1	1	OS	1	1	1	1	1	1	1	1	1	1a	1	6/6	1	1	1	1	1	1	1	1	1
							OD	1	1	2	2	2	1	1	1	1	1a	2	6/24	1	1	2	1	1	1	1	1	1
31	Subbulaxmi	45	F	2	1	2	OS	1	1	2	2	2	1	1	1	1	1a	2	6/24	1	1	2	1	1	1	1	1	1
							OD	1	1	1	1	1	1	1	1	1	1a	1	6/12	1	1	2	1	1	1	1	1	1
32	Sairam	26	M	1	1	1	OS	1	1	1	1	1	1	1	1	1	1a	1	6/12	1	1	2	1	1	1	1	1	1
							OD	1	1	1	1	1	1	1	1	1	1a	1	6/6	1	1	1	1	1	1	1	1	1
33	Rajalaxmi	29	F	1	1	1	OS	1	1	1	1	1	1	1	1	1	1a	1	6/6	1	1	1	1	1	1	1	1	1
								2	3	9	9	9	2	4	1	1	1	6	7	0	1	20	0	1	1	7	3	4

MASTER CHART INDEX

		1	2	3	4	5	6	
1	Ocular Manifestaton	Absent	Present					
2	Eyebrows/Lids	Normal	Abnormal					
3	Conjunctiva	Normal	Congestion					
4	Tear Film Level	Normal	Abnormal					
5	Breakup time	Normal	Abnormal					
6	Schrimer Strip	Normal	Abnormal					
7	Sclera	Normal	Scleritis					
8	Cornea	Normal	Keratitis					
9	Anterior Chamber	Normal	Flare/ cells					
10	Iris	Normal	Iritis					
11	Pupil size	Normal	Miotic	Dilated				
	Reaction	a - Present	b - absent					
12	Lens	Clear	PCC	Immature Cataract	Mature Cataract	Aphakia	Intra Ocular Lens	
13	Tension	Normal	Raised	Decreased				
14	Fields & Colour Visio	Normal	Abnormal					
15	Vitreous	Normal	Vitritis					
16	Disc	Normal	Edematous	atropy				
17	Macular	Normal	Abnormal					
18	Vessels	Normal	Narrowed	Venis dilated	Sheathing			
19	Background Retina	Normal	Haemorrages	Cotton wool spots	Hard exudates			
20	Renal Disease	Absent	Present					

MASTER CHART

Serial No.	Name	Age	Sex	Ocular Manifestation	Ocular symptoms	Renal disease	Eye	Eyebrows/Lids	Conjunctiva	Tear film level	Break up time	Schrimer's Strip	Sclera	Cornea	Anterior Chamber	Iris	Pupil	Lens	Visual acutiy	Tension	Fields/Colour vision	Refractive error	Orbit+Adnexa	Fundus				
																								Vitreous	Disc	Vessels	macula	Background retina
1	Jayalakshmi	22	F	2	1	1	OD	1	1	2	2	2	1	2	1	1	1a	1	6/9	1	1	1	1	1	1	1	1	1
							OS	1	1	2	2	2	1	2	1	1	1a	1	6/9	1	1	1	1	1	1	1	1	1
2	Vijiya	13	F	2	1	2	OD	1	1	1	1	1	1	1	1	1	1a	1	6/12	1	1	2	1	1	1	2	1	1
							OS	1	1	1	1	1	1	1	1	1	1a	1	6/6	1	1	2	1	1	1	2	1	1
3	Santi	34	F	2	1	1	OD	1	1	2	2	2	1	1	1	1	1a	1	6/12	1	1	2	1	1	1	1	1	1
							OS	1	1	1	1	1	1	1	1	1	1a	1	6/6	1	1	2	1	1	1	1	1	1
4	Jayanthi	31	F	2	1	1	OD	1	1	1	1	1	1	1	1	1	1a	1	6/6	1	1	1	1	1	1	1	1	4
							OS	1	1	1	1	1	1	1	1	1	1a	1	6/6	1	1	1	1	1	1	1	1	4
5	Alagu	28	F	2	1	2	OD	1	1	1	1	1	1	1	1	1	1a	1	6/24	1	1	2	1	1	1	4	2	2
							OS	1	2	1	1	1	1	2	2	2	1a	1	6/24	1	1	2	1	1	1	4	2	2
6	Rajathi	30	F	1	1	1	OD	1	1	1	1	1	1	1	1	1	1a	1	6/6	1	1	1	1	1	1	1	1	1
							OS	1	1	1	1	1	1	1	1	1	1a	1	6/6	1	1	1	1	1	1	1	1	1
7	Geetha	20	F	2	1	1	OD	1	1	1	1	1	1	1	1	1	1a	1	6/36	1	2	2	1	2	2	1	1	1
							OS	1	1	1	1	1	1	1	1	1	1a	1	6/36	1	2	2	1	2	2	1	1	1
8	Sulekha Banu	22	F	2	2	1	OD	1	1	2	2	2	1	2	1	1	1a	1	6/6	1	1	1	1	1	1	1	1	1
							OS	1	1	2	2	2	1	2	1	1	1a	1	6/6	1	1	1	1	1	1	1	1	1
9	Jayanthi	32	F	2	1	2	OD	1	1	1	1	1	1	1	1	2	2b	1	6/12	1	1	2	1	1	1	1	1	1
							OS	1	1	1	1	1	1	1	1	2	2b	1	6/6	1	1	2	1	1	1	1	1	1
10	Latha	30	F	2	1	1	OD	1	1	2	1	2	1	1	1	1	1a	2	6/12	1	2	2	1	1	1	1	2	1
							OS	1	1	2	1	2	1	1	1	1	1a	2	6/12	1	2	2	1	1	1	1	2	1
11	Lalitha	17	F	1	1	1	OD	1	1	1	1	1	1	1	1	1	1a	1	6/9	1	1	2	1	1	1	1	1	1
							OS	1	1	1	1	1	1	1	1	1	1a	1	6/9	1	1	2	1	1	1	1	1	1
12	Latha	16	F	1	1	1	OD	1	1	1	1	1	1	1	1	1	1a	1	6/6	1	1	1	1	1	1	1	1	1
							OS	1	1	1	1	1	1	1	1	1	1a	1	6/6	1	1	1	1	1	1	1	1	1
13	Murugan	30	M	2	1	2	OD	1	1	1	1	1	2	1	1	1	1a	1	6/24	1	1	2	1	1	1	2	1	2,3
							OS	1	1	1	1	1	1	1	1	1	1a	1	6/12	1	1	2	1	1	1	2	1	2,3
14	Poorna	11	F	2	1	1	OD	2	1	1	1	1	1	1	1	1	1a	1	6/9	1	1	2	1	1	1	1	1	1
							OS	2	1	1	1	1	1	1	1	1	1a	1	6/9	1	1	2	1	1	1	1	1	1
15	Amasavally	35	F	1	1	2	OD	1	1	1	1	1	1	1	1	1	1a	1	6/6	1	1	1	1	1	1	1	1	1
							OS	1	1	1	1	1	1	1	1	1	1a	1	6/6	1	1	1	1	1	1	1	1	1
16	Firudos Banu	19	F	1	1	1	OD	1	1	1	1	1	1	1	1	1	1a	1	6/6	1	1	1	1	1	1	1	1	1
							OS	1	1	1	1	1	1	1	1	1	1a	1	6/6	1	1	1	1	1	1	1	1	1
17	Uma	35	F	2	1	1	OD	1	1	1	1	1	1	1	1	1	1a	2	6/36	1	1	2	1	1	1	1	1	1
							OS	1	1	1	1	1	1	1	1	1	1a	2	6/36	1	1	2	1	1	1	1	1	1